

Cezox

(Cefixime USP)

سیزوکس
(سیفیکزائم یو۔ایس۔پی)

COMPOSITION

Each **Cezox** 400mg capsule contains Cefixime 400mg.
Each 5ml of **Cezox** reconstituted suspension contains Cefixime 100mg.
Each 5ml of **Cezox DS** reconstituted suspension contains Cefixime 200mg.

MECHANISM OF ACTION

Bactericidal action of Cefixime results from inhibition of cell-wall synthesis.

PHARMACOKINETICS

Absorption: Cefixime suspension, given orally, is about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food. Food reduces the absorption following administration of the capsule by approximately 15% based on AUC and 25% based on C_{max}. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension. Peak serum concentrations occur between 3 and 8 hours following oral administration of a single 400 mg capsule.

Distribution: Serum protein binding is concentration independent with a bound fraction of approximately 65%. Adequate data on CSF levels of Cefixime are not available.

Metabolism and Excretion: There is no evidence of metabolism of Cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. The serum half-life of Cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours.

Renal Impairment: In subjects with moderate impairment of renal function (20 to 40 mL/min creatinine clearance), the average serum half-life of Cefixime is prolonged to 6.4 hours. In severe renal impairment (5 to 20 mL/min creatinine clearance), the half-life increased to an average of 11.5 hours. The drug is not cleared significantly from the blood by hemodialysis or peritoneal dialysis.

MICROBIOLOGY

Cefixime has been shown to be active against most isolates of the following bacteria both in vitro and in clinical infections:

Gram-positive bacteria	Gram-negative bacteria
Streptococcus pneumoniae	Haemophilus influenzae
Streptococcus pyogenes	Moraxella catarrhalis
	Escherichia coli
	Proteus mirabilis
	Neisseria gonorrhoeae

INDICATIONS

Cefixime is a cephalosporin antibacterial indicated in the treatment of adults and pediatric patients six months of age or older with the following infections when caused by susceptible isolates of the designated bacteria:

- Uncomplicated Urinary Tract Infections
- Otitis Media
- Pharyngitis and Tonsillitis
- Acute Exacerbations of Chronic Bronchitis
- Uncomplicated Gonorrhea (cervical/urethral)

DOSAGE AND ADMINISTRATION

Adult: The recommended dose of Cefixime is 400 mg daily, administered without regard to food. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of Cefixime should be administered for at least 10 days.

Pediatric Patients (6 months or older): The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours.

PEDIATRIC DOSAGE CHART

		100 mg/5 mL	200 mg/5 mL
Patient Weight	Dose/Day	Dose/Day	Dose/Day
(kg)	(mg)	(mL)	(mL)
5 to 6.2	50	2.5	1.25
6.3 to 12.5	100	5	2.5
12.6 to 18.8	150	7.5	3.75
18.9 to 25	200	10	5
25.1 to 31.3	250	12.5	6.25
31.4 to 37.5	300	15	7.5
37.6 to 43.8	350	17.5	8.75
43.9 to 50	400	20	10

Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose. Otitis media should be treated with the suspension. Clinical trials of otitis media were conducted with the suspension. Therefore, the capsule should not be substituted for the suspension in the treatment of otitis media.

Renal Impairment: Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater. Patients whose clearance is between 21 and 60 mL/min or patients who are on renal hemodialysis may be given 6.5 mL of Cefixime for Oral Suspension (200 mg/5 mL) daily or 13 mL of Cefixime for Oral Suspension (100 mg/5 mL) daily. Patients whose clearance is 20 mL/min or less, or patients who are on continuous ambulatory peritoneal dialysis may be given 200 mg daily. Neither hemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.

ADVERSE EFFECTS

The most commonly seen adverse reactions were gastrointestinal events, which were reported in 30% of adult patients on either the twice daily or the once daily regimen. Five percent (5%) of patients in clinical trials discontinued therapy because of drug-related adverse reactions. Individual adverse reactions included diarrhea 16%, loose or frequent stools 6%, abdominal pain 3%, nausea 7%, dyspepsia 3%, and flatulence 4%. The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in pediatric patients receiving the suspension was comparable to the incidence seen in adult patients. Post-marketing Experience. The following adverse reactions have been reported following the use of Cefixime. Incidence rates were less than 1 in 50 (less than 2%).

Gastrointestinal: Several cases of documented pseudomembranous colitis were identified in clinical trials.

The onset of pseudomembranous colitis symptoms may occur during or after therapy.

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported.

Hepatic: Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice.

Renal: Transient elevations in BUN or creatinine, acute renal failure.

Central Nervous System: Headaches, dizziness, seizures.

Hemic and Lymphatic System: Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.

Abnormal laboratory tests: Hyperbilirubinemia.

Other Adverse Reactions: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis. Adverse reactions reported for cephalosporin-class drugs: Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

WARNINGS AND PRECAUTION

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of Cefixime. Before therapy with Cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to Cefixime occurs, discontinue the drug.

Clostridium difficile-Associated Diarrhea: *Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Coagulation Effects: Cephalosporins, including Cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Development of Drug-Resistant Bacteria: Prescribing Cefixime in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

DRUG INTERACTIONS

Carbamazepine: Elevated carbamazepine levels have been reported in postmarketing experience when Cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants: Increased prothrombin time, with or without clinical bleeding, has been reported when Cefixime is administered concomitantly.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery: Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

Nursing Mothers: It is not known whether Cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

Pediatric Use: Safety and effectiveness of Cefixime in children aged less than six months old have not been established.

Geriatric Use: A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters. These differences were small and do not indicate a need for dosage adjustment of the drug in the elderly.

CONTRAINDICATIONS

Cefixime is contraindicated in patients with known allergy to Cefixime or other cephalosporins.

OVERDOSAGE

Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2 g of Cefixime did not differ from the profile seen in patients treated at the recommended doses.

PRESENTATION

Cap. **Cezox** 400 mg : 5's/pack.
Susp. **Cezox** 100mg/5ml : 1's/pack.
Susp. **Cezox DS** 200mg/5ml : 1's/pack.

دوا تیار کرنے کا طریقہ:
سپین تیار کرنے کے لئے پہلے بال کرکھٹا کرنا ہوگا پانی بول پر دیئے گئے نشان

تک ڈالیں اور اچھی طرح ملائیں تاکہ گریڈ 200mg/5ml ہو جائے۔

تیار شدہ سپین کو سات دن کے اندر استعمال کریں۔

خوراک:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

DOSAGE: As directed by the physician

INSTRUCTIONS

To be sold on the prescription of registered medical practitioner only.

Shake the bottle before use and tightly close after use.

Improper storage may deteriorate the medicine.

Protect from heat, light & moisture.

Keep all medicines out of the reach of children.

Store below 30°C. For oral use only.

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Detailed prescribing information is available on request.



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